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TITLE: A Randomized Placebo-Controlled Trial of Citalopram for Anxiety Disorders
Following Traumatic Brain Injury

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14. ABSTRACT The overarching goal of this project is to study the effects of a serotonin reuptake inhibitor (SRI), citalopram, for the treatment of anxiety experienced by individuals after traumatic brain injury (TBI). Specifically, this project seeks to treat individuals who meet criteria for DSM-IV diagnosis of Anxiety Disorder Due to a General Medical Condition, within 6 to 24 months of TBI. A randomized placebo controlled design with 1-year follow-up will be utilized to evaluate the effectiveness of citalopram in alleviating significant anxiety symptoms that cause significant distress and can lead to medical retirement of active duty soldiers.					
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Introduction:

The overarching goal of this project is to determine the effectiveness of citalopram for the treatment of anxiety disorders following Traumatic Brain Injury (TBI) and to examine possible longer term effectiveness of treatment with citalopram on symptom reporting and return to work/duty.

Body:

Participants who experienced a TBI 6 to 24 months ago and are experiencing anxiety are eligible for the study. If they agree to participate, they will sign informed consent prior to research testing. An informational script about the study is read to individuals. After the script is read, the individual will be given the informed consent to review. Patients will not be eligible to participate in the study until they reach a Rancho Los Amigos level of 7 or 8. If there is any question as to a patient's capacity to consent, the neuropsychologist and/or psychiatrist involved in the study will assess the subject's level of comprehension prior to consent. Any confusional state prohibits a subject from being rated as a 7 or 8. After signing the informed consent, tests and scales will be administered and patients will be randomized to receive a 12-week course of citalopram or placebo. Female participants of childbearing potential will be given a serum pregnancy test prior to randomization. If the test is positive, she will not be allowed to participate.

Eligible, consented participants will receive an increasing dose of citalopram or placebo up to a dose of 40 mg of citalopram or 4 pills of placebo. A blood sample drawn after completion of the 12-week treatment period will be used to obtain citalopram levels as a measure of medication compliance. A two-week taper will follow the treatment period. Study participants will receive comprehensive multidisciplinary evaluations at a DVBIC site, including neuropsychological and psychiatric interviews and evaluations at baseline, 12 weeks and 12 months.

There have been no modifications made to the technical approach section of the protocol.

The number of subjects enrolled (or specimens used) in the study since last APR in the multi-center study is 14. The total number of subjects enrolled over the entire study length is 15.

Since the last APR, an addendum has been approved at six of the seven sites involved in the multi-center study to extend the study window from 14 months post injury to 24 months. This change was made when it became clear that patients the DVBIC was seeing clinically were either very acutely injured or more than one year post injury.

An additional addendum was submitted and approved to use an advertisement as a recruitment strategy for potential subjects (See Appendix). The advertisement is currently being used at six of the seven participating study sites.

A remote data entry system was implemented for this protocol and has been very successful in permitting real time quality improvement and monitoring of study data. Each of the four sites who have enrolled subjects has been actively entering patient data into the electronic data capture system in a timely fashion.

Key Research Accomplishments:

- Received protocol IRB approval from the James A. Haley VA Hospital (JAHVAH) in Tampa, Florida and the Human Subjects Research Review Board (HSRRB) at Ft. Detrick. Tampa became the sixth site to receive approval and begin participating in the study.
- Enrolled 14 new subjects in the study.
- Began utilizing electronic data capture system to maintain case report forms and monitor patient progress through study.

Reportable Outcomes:

A poster presentation was made in May 2006 at the 2006 Department of Defense Military Health Research Forum. The poster provided an update on the study's progress to date, along with initial characterization of study participants.

Conclusion:

Though there have been some challenges in patient accrual, many steps have been taken to increase patient accrual. This study remains the only large pharmaceutical study of anxiety disorders following TBI. Our goal is to enroll the remaining 89 patients in the next 1 ½ years.

No research conclusions can be made at this time.

References:

Not Applicable

Appendix - see page 6

Are you or someone you know feeling anxious following a head injury?

If so you may be eligible to participate in a clinical research study testing a medication for the treatment of anxiety, which may occur following a head injury.

Have you had a head injury between 6 and 24 months ago and are you:

- ✓ **Between the ages of 18 and 65?**
- ✓ **A military healthcare beneficiary?**
- ✓ **Experiencing anxiety?**
- ✓ **Able to read English and follow simple instructions?**

If you are qualified, you may be enrolled in this study which includes 12 weeks of drug therapy and 12 months of follow-up, and receive study-related evaluations and medication.

**If you or someone you know may be interested in participating, please contact Stephanie Ball at the Defense and Veterans' Brain Injury Center in Building 2 at Walter Reed Army Medical Center
800-870-9244 or 202-782-3057
Principal Investigator: Deborah Warden, MD**

The possible benefit to you from being in this study is that you may feel and function better. However, no benefit can be guaranteed. The information we learn may be helpful to future individuals with brain injury.